

REMARKS

These remarks are in response to the Office Action dated February 4, 2002. Claims 1-6 and 8 have been amended. Claims 9-17 have been added. Support for the amended and new claims can be found throughout the specification. No new matter has been added. Claims 1-6 and 8-17 are pending and at issue. Attached is a marked-up version of the changes being made by the current amendment. Applicants respectfully request reconsideration of the present application.

Claim Objections

Claims 3 and 8 are objected to as lacking periods. Applicant notes that claims 3 and 8 have been amended so as to include periods. In view of the amendments to the claims, Applicant submits that the present objection is moot and respectfully requests its withdrawal.

Drawing Objections

The Office Action provides an "Attachment for PTO-948." However, a PTO-948 form was not provided with the present Office Action as received by Applicant's representative. Applicant respectfully requests that the Draftsman provide the PTO-948 form so that Applicant may respond to any concerns regarding the formal drawings filed with the application.

I. REJECTION UNDER 35 U.S.C. §101

Claims 4-8 stand rejected under 35 U.S.C. §101 because the claimed invention is directed to non-statutory subject matter. Applicants note that this rejection is moot with regard

to canceled claim 7. Applicants further note that amended dependent claims 5, 6 and 8 now depend from claim 2. Applicants respectfully traverse this rejection as it may apply to claim 4.

Specifically, the Office Action states that the claims recite no process steps and therefore are drawn to a use. Applicants note that claim 4 has been amended to recite the process steps of contacting a fluid with a lipid membrane of the invention, wherein the membrane is associated with an acidic compound capable of modifying the pH of the fluid. In view of the amendments to the claims the claimed invention is clearly directed to statutory subject matter. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §101, be withdrawn.

II. REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-8 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants note that this rejection is moot with regard to canceled claim 7. Applicants respectfully traverse this rejection as it may apply to the amended claims.

Specifically, the Office Action states that the term "small" is unclear. Applicants note that "small" has been deleted from the claims. The Office Action further states that claim 4 fails to recite method steps. Applicant notes that claim 4 has been amended to clarify the method of the claimed invention. The Office Action further states that "said hybrid mixture," as recited in claim 8, lacks antecedent basis. Claim 8 has been amended to depend from claim 6 which provides the

appropriate antecedent basis for pending claim 8. Similarly, claim 6 has been amended to depend from claim 2 which provides the appropriate antecedent basis for pending claim 6. Finally, claim 1 has been amended to recite process steps.

In view of the amendments to the claims, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

III. REJECTIONS UNDER 35 U.S.C. §103

Claims 4-7 stand rejected under 35 U.S.C. §103(a) as being obvious over Williams in view of Wheatley et al. Applicant notes that this rejection is moot with regard to canceled claim 7. Applicants respectfully traverse this rejection as it may apply to the amended claims.

Specifically, the Office Action states that Williams discloses the use of liposomes for renal dialysis and that Wheatley discloses the encapsulation of a liposome via alginate cross-linking. Applicants note that claim 4 has been amended to recite contacting a fluid with a "lipid membrane prepared by the method claim 2." Claim 2 recites, in part, a method for preparing a lipid membrane comprising "silyl lipid molecules ... wherein each silyl lipid molecule comprises at least one silanol group." Claim 2 further recites "cross-linking, via a siloxane bond, at least one silanol group from a first silyl lipid with at least one silanol group from a second silyl lipid." In contrast, neither Williams nor Wheatley disclose the use of such groups or the method of cross-linking provided by the claimed invention.

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Accordingly, Applicant respectfully requests reconsideration and withdrawal of the pending rejection under 35 U.S.C. §103(a).

Conclusion

In summary, for the reasons set forth herein, Applicants maintain that claims 1-6 and 8-17 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' representative can be reached at (858) 678-5070. Payment of the one-month extension fee set forth in 37 CFR §1.17(a)(2) is submitted herewith. Please charge any additional fees, or make any credits, to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 10/18/02



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Version with markings to show changes made

In the claims:

Claim 7 has been canceled.

Claims 1-6 and 8 have been amended as follows:

1. (Amended) A method of preparing a lipid membrane [sol-gel encapsulated phospholipids vesicles], the method comprising:

(a) [sonicating an aqueous solution of a phospholipid to form a solution of multilamellar vesicles] providing a lipid membrane comprising a lipid monolayer, bilayer or multilayer;

(b) [freezing and thawing said solution of step (a) at least five times] providing a plurality of silyl lipid molecules integrally-associated with the lipid membrane of (a), wherein each silyl lipid molecule comprises at least one silanol group;
and

(c) [filtering said solution of step (b) to form a solution of small unilamellar vesicles; and] cross-linking, via a siloxane bond, at least one silanol group from a first silyl lipid with at least one silanol group from a second silyl lipid

[(d) curing said solution of step (c) for at least one day].

2. (Amended) A method of preparing [sol-gel] an encapsulated Langmuir lipid membrane, [vesicles] the method comprising:

(a) [sonicating an aqueous acidic solution of a silyl lipid, or a mixture of a silyl lipid and a phospholipid, to form a solution of multilamellar vesicles] providing a lipid monolayer, bilayer or multilayer membrane comprising a plurality of silyl lipid molecules integrally-associated with the lipid

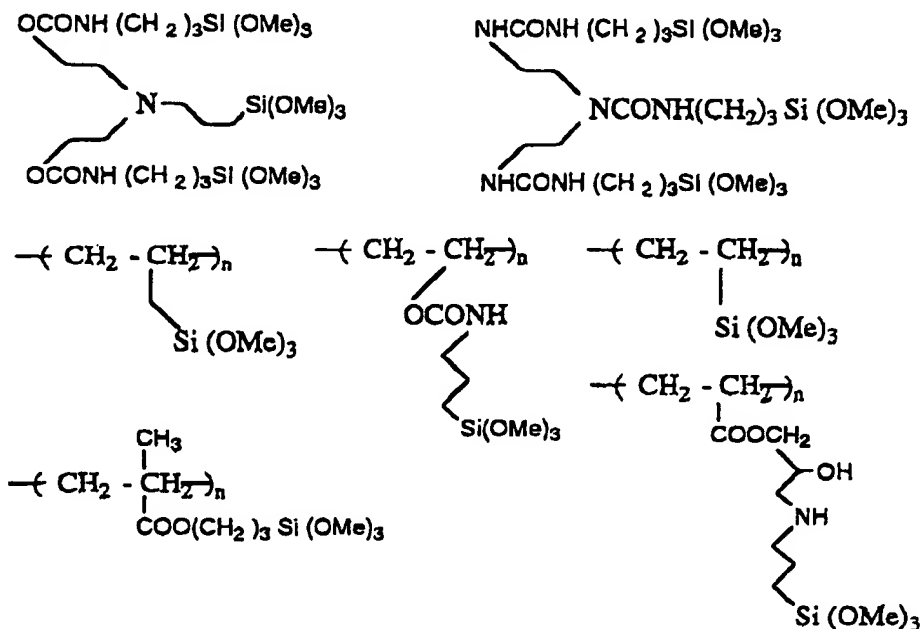
monolayer, bilayer or multilayer membrane, wherein each silyl lipid molecule comprises at least one silanol group;

(b) [filtering said solution of multilamellar vesicles of step (a) to form a solution of small unilamellar vesicles] cross-linking, via a siloxane bond, at least one silanol group from a first silyl lipid with at least one silanol group from a second silyl lipid;

(c) [mixing said small unilamellar vesicles of step (b) with a solution of inorganic-organic hybrid mixture sol] providing an upper layer of encapsulation material; and

(d) [curing the solution of step (d) for at least one day] providing a lower layer of encapsulation material or a lower layer of supporting substrate;

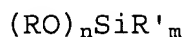
[said vesicles comprising silyl lipid or a mixture of silyl lipid and phospholipids] wherein the lipid monolayer, bilayer or multilayer membrane is positioned between the upper layer and the lower layer.

$$\begin{aligned} &(\text{MeO})_3\text{Si}(\text{CH}_2)_2\text{Si}(\text{OMe})_3 \\ &(\text{EtO})_3\text{SiCH}_2\text{CH}_2\text{CH}_2)_2\text{NH} \\ &(\text{MeO})_3\text{Si}(\text{CH}_2)_3\text{NH}(\text{CH}_2)_2\text{NH}(\text{CH}_2)_3\text{Si}(\text{OMe})_3 \\ &(\text{MeO})_3\text{Si}(\text{CH}_2)_3\text{NHCONH}(\text{CH}_2)_3\text{Si}(\text{OMe})_3 \\ &(\text{MeO})_3\text{Si}(\text{CH}_2)_3\text{NHCOO}(\text{CH}_2\text{CH}_2\text{O})_n\text{CONH}(\text{CH}_2)_3\text{Si}(\text{OMe})_3 \quad n=1,2,3,4 \end{aligned}$$


4. (Amended) A method of modifying the pH of a fluid comprising plasma and suspended formed elements, [performing renal dialysis by using sol-gel encapsulated lipid vesicles; said lipid vesicles comprised of phospholipid, silyl lipid or a mixture of phospholipid and silyl lipid, said lipid vesicles being positioned in the sol-gel encapsulation material] the method comprising contacting the fluid with a lipid membrane

prepared by the method claim 2, wherein the lipid membrane is associated with an acidic compound capable of modifying the pH of the fluid.

5. (Amended) The method of claim [4] 2 wherein said silyl lipid is of the formula:



wherein:

R is selected from a group consisting of C₁-C₅₀ alkyl;

R' is selected from a group consisting of (CH₂)_qA and OSiR₃;

A is selected from a group consisting of hydrogen, COO⁻, OH, COOH, N⁺R₁R₂R₃, NHR'', SH, SR'' and C₁-C₅₀ alkyl;

R₁, R₂, R₃ and R'' are selected from a group consisting of (CH₂)_qCH₃ and (CH₂)_qSi(OR)₃;

q is a number from 1 to 50;

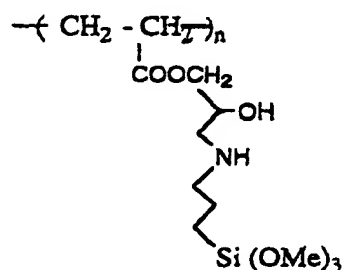
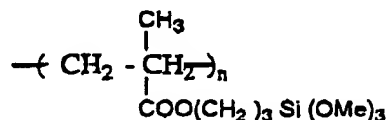
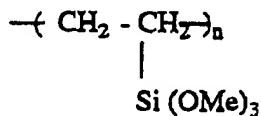
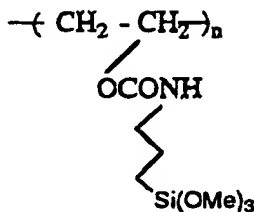
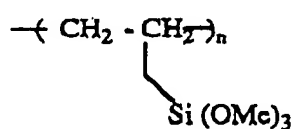
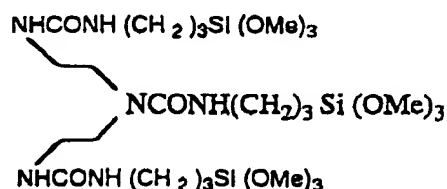
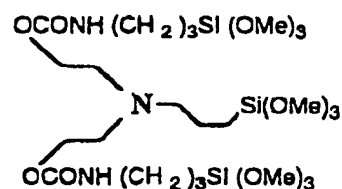
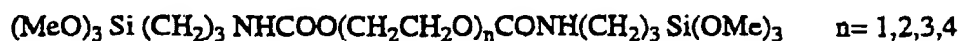
n is a number from 1 to 4; and

m is a number from zero to 3.

6. (Amended) The method of claim [4] 2 wherein said [sol-gel] encapsulation material is an inorganic-organic hybrid mixture sol.

7. (Canceled) The method of claim 6 wherein said inorganic-organic hybrid mixture sol-gel is a gel formed from an inorganic-organic hybrid mixture sol solution.

8. (Amended) The method of claim [4] 6 wherein said hybrid mixture sol[-gel] is prepared from precursor molecules of the following formula:



Please add the following new claims:

9. A method for stabilizing a lipid membrane, the method comprising:

a) providing a lipid membrane comprising a lipid monolayer, bilayer or multilayer;

b) providing a plurality of silyl lipid molecules integrally-associated with the lipid membrane of a), wherein each silyl lipid molecule comprises at least one silanol group; and

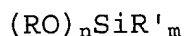
c) cross-linking, via a siloxane bond, at least one silanol group from a first silyl lipid with at least one silanol group from a second silyl lipid,

thereby stabilizing the lipid vesicle.

10. The method of claim 9, wherein the lipid membrane comprises phospholipids.

11. The method of claim 9, wherein the lipid membrane further comprises a protein.

12. The method of claim 9, wherein the silyl lipid is of the formula:



wherein:

R is selected from a group consisting of C₁-C₅₀ alkyl;

R' is selected from a group consisting of (CH₂)_qA and OSiR₃;

A is selected from a group consisting of hydrogen, COO⁻, OH, COOH, N⁺R₁R₂R₃, NHR'', SH, SR'' and C₁-C₅₀ alkyl;

R₁, R₂, R₃ and R'' are selected from a group consisting of (CH₂)_qCH₃ and (CH₂)_qSi(OR)₃;

q is a number from 1 to 50;

n is a number from 1 to 4; and

m is a number from zero to 3.

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13. The method of claim 9, wherein the lipid membrane forms a vesicle.

14. The method of claim 9, wherein the silyl lipids are further cross-linked to an encapsulation material.

15. The method of claim 14, wherein the encapsulation material is selected from the group consisting of sol-gel matrix, hybrid mixture sol-gel matrix and glass matrix.

16. The method of claim 14, wherein the sol-gel matrix is an inorganic-organic hybrid mixture sol.

17. The method of claim 15 wherein the hybrid mixture sol-gel matrix is prepared from precursor molecules of the following formula:

